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COORDINATE-BASED META-ANALYTIC SEARCH FOR THE SPM NEUROIMAGING PIPELINE

The BredeQuery plugin for SPM5

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Abstract: Large amounts of neuroimaging studies are collected and have changed our view on human brain function. By integrating multiple studies in meta-analysis a more complete picture is emerging. Brain locations are usually reported as coordinates with reference to a specific brain atlas, thus some of the databases offer so-called coordinate-based searching to the users (e.g. Brede, BrainMap). For such search, the publications, which relate to the brain locations represented by the user coordinates, are retrieved. In this paper we present BredeQuery – a plugin for the widely used SPM5 data analytic pipeline. BredeQuery offers a direct link from SPM5 to the Brede Database coordinate-based search engine. BredeQuery is able to ‘grab’ brain location coordinates from the SPM windows and enter them as a query for the Brede Database. Moreover, results of the query can be displayed in an SPM window and/or exported directly to some popular bibliographic file formats (BibTeX, Reference Manager, etc).

1 INTRODUCTION

The growing number of functional neuroimaging studies of increasingly sophisticated human brain activity brings the demand for new tools/services for integration of research findings, wider exchange of information between laboratories from the same research area and efficient searching of related articles, reviews and other literature (Wager et al., 2007).

The dominant paradigm in current neuroimaging is that of *functional localization*. Functional localization hypothesizes that a given human behavior is established by a change in brain activity in a relatively limited number of spatially segregated processing units. Thus the result of an experiment under this paradigm consists of a Statistical Parametric Map (SPM) indicating the local involvement. Often the SPM is summarized as a list of regions, see e.g., (Friston et al., 2007; Pekar, 2006), in which the SPM has been judged to be significantly different from zero (regions were the null hypothesis is rejected). As the typical neuroimaging experiment investigates a highly controlled behavior and often involves a rela-

tively limited number of subjects, there is strong need for tools to integrate multiple experiments in order to increase the robustness to the experiment specific implementation of the given behavior and to statistical fluctuation due to limited sample sizes.

Several methods have been proposed for neuroimaging meta-analysis and for estimation of associations between the brain locations and textual representations of behavior, for a recent review, see e.g., (Wager et al., 2007). A set of methods are based on the so-called Brede Database (Nielsen, 2003). Methods for integration include estimation of conditional probability density functions representing the localized probability of activation in response to a given behavior ‘word’ (Nielsen and Hansen, 2002; Nielsen and Hansen, 2004) and multivariate methods based on non-negative matrix factorization that aim to represent global dependencies between brain activation and semantic text labels from neuroscience publications (Nielsen et al., 2004).

Brain locations are reported as region coordinates relative to a specific brain atlas (usually MNI or Talairach spaces), hence, there is an interest for effec-

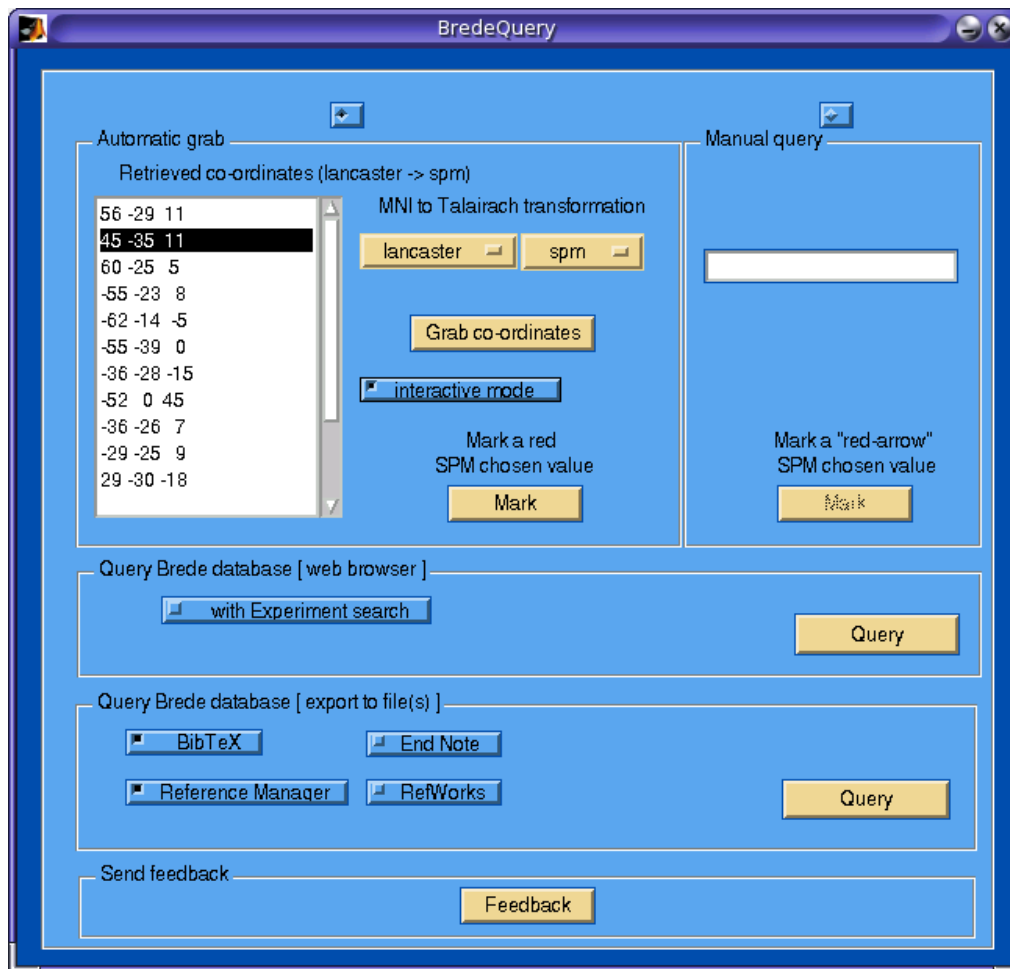


Figure 1: Graphical user interface of the BredeQuery plugin for SPM5. Firstly, the user can choose if the coordinates used for querying will be grabbed from an SPM's results window or will be typed manually. The grabbed (retrieved) coordinates are shown on the list. The user can switch on an interactive mode – the coordinate selected in the SPM window will be automatically selected in the plugin on the coordinates list. Moreover, the coordinates are grabbed using the chosen MNI to Talairach transformation (Brett or Lancaster MTT affine transformations). Afterwards, the user is able to display the query results in the Matlab web browser or to import them into the specified bibliographic format.

tive search for experiments, hence, scientific papers, which report similar coordinate sets in brain. Brain-Map (Laird et al., 2005) and Brede (Nielsen, 2003) are the databases which offer the coordinate-based searching. For Brede it is available on both the web-page and in a standalone application.

In order to enable a neuroimaging scientists to perform meta-analysis in the context of a specific ongoing study we here propose a tool that integrates retrieval of related research within the data analysis pipeline. The dominant tool for human brain mapping is undisputable the SPM set of tools developed and distributed by the Functional Imaging Laboratory (London, (Friston et al., 2007)). For an analysis of the usage of imaging pipelines see e.g., (Nielsen et al.,

2006). Thus we have initiated the development of a *plugin* for SPM5, which offers high integration with the Brede Database.

The *BredeQuery plugin* (see Figure 1) provides the opportunity to perform coordinate-based query and retrieval of the related articles references directly from the SPM (Matlab) environment.

2 BREDE DATABASE

The Brede Database available through the web-page: <http://hendrix.imm.dtu.dk/services/jerne/brede/> records published neuroimaging experiments that list

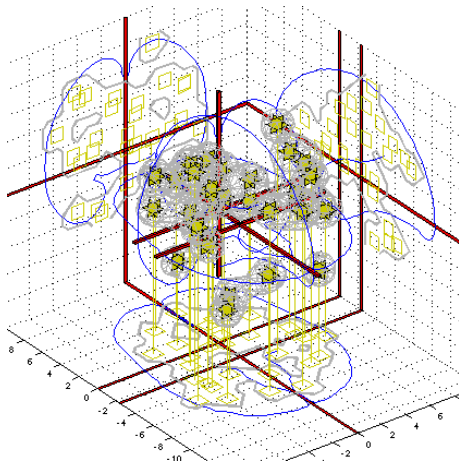


Figure 2: Screenshot from one of the pages in the Brede Database showing coordinates in Talairach space. This is one of presently 586 experiments recorded in the database – an fMRI experiment resulting in 29 reported coordinates.

stereotaxic coordinates in so-called MNI or Talairach space (Talairach and Tournoux, 1988). Presently, close to 4000 coordinates from 186 papers with a total of 586 experiments are available.

The data is stored in XML files, and Matlab functions generate static webpages with visualization of the entries in the database, see Figure 2. Web-based searching is possible from the homepage, but up till now it has required that the researcher manually typed in the query or extracted results from the image analysis program. Webpages are also available with the Brede Database ontologies, which exist for brain regions and brain functions, see Figure 3.

3 RELATED TOOLS

There are a few available tools that have aims related to those of the BredeQuery plugin.

The AMAT SPM toolbox is also meta-analysis toolbox (Hamilton, 2005) for Matlab based meta-analysis of fMRI data. It provides coordinate-based search for over 5000 coordinates from 213 published papers of which some were derived from the Brede Database. The coordinates are in MNI or Talairach space. The toolbox can locate neighboring coordinates to a given coordinate, as well as publications for a given author or year. The tool was last updated in 2005.

Another related toolbox, is xjView (Cui and Li, 2007), which offers the SPM user, apart from viewing the images in glass view, section view or 3D render view, search of selected

brain regions in databases in order to elucidate their function. It searches among others in Google Scholar (<http://scholar.google.com/>), PubMed (<http://www.ncbi.nlm.nih.gov/pubmed/>) and the xBrain database, available on the webpage: <http://sig.biostr.washington.edu/projects/xbrain/>.

The XCEDE SPM Toolbox (Keator et al., 2006) is also a toolbox distributed within the SPM community. This is a toolbox for SPM99 and SPM2, which enables the users to capture activation data for PET/fMRI analysis and save them to the XML file in a XCEDE XML schema. Moreover, it is extending the exported XML file by adding automatically the anatomical labeling of the region in the brain for the given activity coordinates. It is achieved through two SPM toolboxes: Talairach Daemon available on <http://www.talairach.org/> and Automated Anatomical Labeling (AAL) available on <http://www.cyceron.fr/freeware/>.

4 SOFTWARE DESCRIPTION

The recent version of the *BredeQuery* plugin, together with the User's Guide, can be downloaded from the webpage: <http://neuroinf.imm.dtu.dk/BredeQuery/>. A graphical user interface of the BredeQuery plugin is divided into five areas where different user-actions can be performed. Firstly, the activity coordinates can be 'grabbed' from the SPM results figure into the plugin. Since the coordinates can be presented in MNI or Talairach spaces, some transformations are introduced for interoperability. The coordinate-based search in the Brede Database is based on the Talairach space coordinates, thus the BredeQuery plugin offers two MNI to Talairach transformations, which can be chosen by the user. The piece-wise affine transformation proposed by Matthew Brett is one of the available transformation (Brett, 1999). Also included is the affine transformation MNI-to-Talairach (MTT), suggested by Jack Lancaster et al. (Lancaster et al., 2007). Three separate transformation were suggested by the group: one for SPM, one for FSL and a combined 'pooled' transformation. The MTT_{SPM} transformation is set as default in the BredeQuery plugin.

When the coordinates have been 'grabbed' and shown in the BredeQuery plugin, the coordinate-based querying with Brede Database can be done. One or more coordinates can be selected for querying and the results from the Brede Database (publications related to the given activity coordinate) are displayed by the plugin in a web browser (see Figure 5), exported to an XML file or saved in the bibliographic file format (BibTeX, Reference Manager, RefWorks

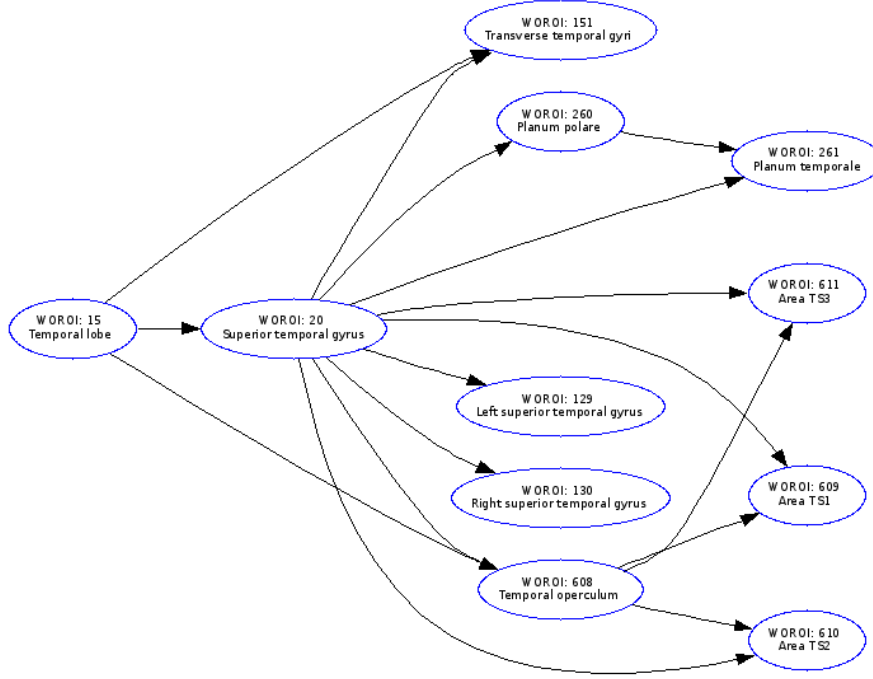


Figure 3: Relationships and taxonomy of the regions in brain associated with superior temporal gyrus. The entire ontologies for brain regions and brain functions are available together with the Brede Database.

or EndNote). We mention that the coordinates need not necessarily be grabbed from SPM in order to make a query. The coordinates can also be entered manually in a manner similar to the functionality on the webpage of the Brede Database.

The user is also able to perform an ‘experiment search’ (available in the Brede Database service) via the BredeQuery. It has previously been suggested how a similarity can be computed between one set of coordinates and a volume or another set of coordinates (Nielsen and Hansen, 2004). This procedure required the conversion of the set of coordinates to a volume by kernel density estimation. It is, however, not necessary to convert the coordinates to a volume if only the similarity between two coordinates sets are to be compared. It will then generally be faster to compute the similarity based on all coordinate-coordinate pair-wise similarities and perform a weighted summation. There are multiple ways to compute the similarity. Presently, the web-service for the Brede Database uses the following Gaussian/Euclidean form

$$s_{q,e} = \frac{1}{\sqrt{N}} \sum_{m=1}^M \sum_{n=1}^N \exp \left(\frac{(x_m^q - x_n^e)^2 + (y_m^q - y_n^e)^2 + (z_m^q - z_n^e)^2}{-2\sigma^2} \right),$$

where σ is set to 10 millimeters, (x_m^q, y_m^q, z_m^q) is the m th of M three-dimensional query coordinates, while (x_n^e, y_n^e, z_n^e) is the n th of N three-dimensional coordinates in the Brede Database. The factor $1/\sqrt{N}$ aims to regularize for the number of coordinates in each set so that sets with many coordinates do not dominate the search result. A corresponding weight for the query coordinates is not necessary, since this factor will be equal for all queried sets of coordinates of the database.

Following the terminology of BrainMap, a set of coordinates is in the Brede Database called an ‘experiment’ (Fox et al., 1994), thus the name ‘experiment search’.

The Perl function that presently provides the search functionality from the Brede Database webpage is part of the Brede Toolbox, and this toolbox is available on the Internet (<http://hendrix.imm.dtu.dk/software/brede/>).

5 EXAMPLE SESSION

In this section we present the example steps for the user session in SPM5 using BredeQuery plugin. The sample data – *Single subject epoch (block) audi-*

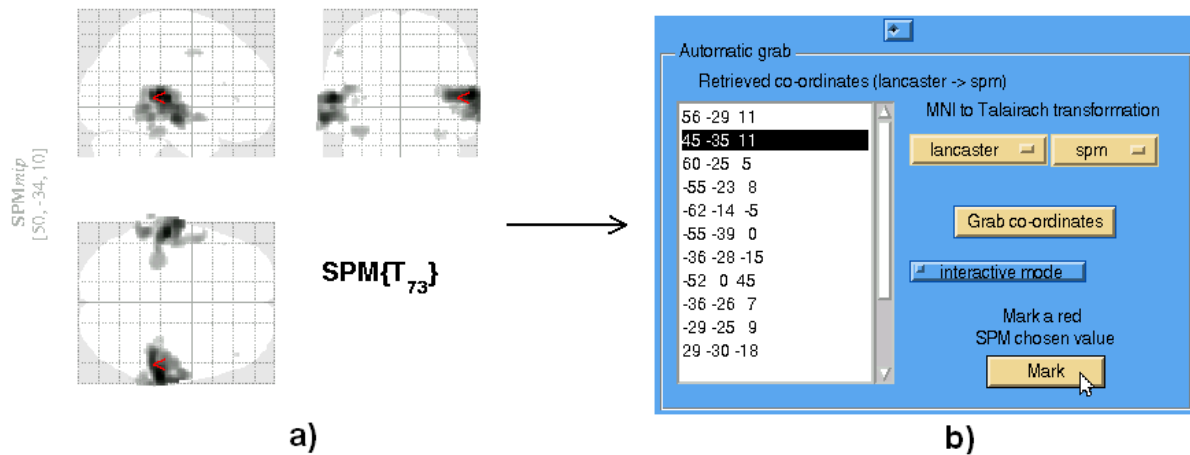


Figure 4: The demonstration of example usage of the BredeQuery plugin in SPM. The user can see regions with significant brain activation in the SPM results window. The region of activation represented by the coordinate (50, -34, 10) in MNI space is selected (a). The same coordinate, transformed to the Talairach space using Lancaster's MTT_{SPM} transformation is marked on the BredeQuery's coordinates list as (45, -35, 11) (b). Afterwards, the user is able to submit coordinate-based queries to the Brede Database and get the articles related to the same (or nearby) brain regions.

tory fMRI activation data, taken from SPM webpage: <http://www.fil.ion.ucl.ac.uk/spm/data/auditory/>, was used for this demonstration purposes. An example SPM5-BredeQuery session may proceed with the following steps:

1. In an analysis of PET/fMRI data with SPM5, the data set is loaded, a statistical analysis is performed and, finally, results are displayed in an SPM window. The regions of significant brain activation are marked and their coordinates can be retrieved. The currently selected activation is marked with a small red arrow. In our example (Figure 4), the user has loaded and analyzed the data. After the analysis, he has selected the activation, represented by the coordinate in the MNI space as (50, -34, 10) – see Figure 4a.
2. The BredeQuery plugin is run by choosing the BredeQuery entry in the SPM's toolbox pop-up menu. All coordinates are grabbed by the plugin and shown in the coordinates list. They are transformed according to the chosen MNI-to-Talairach transformation. In our example, the coordinates were transformed using the Lancaster's MTT_{SPM} affine transformation. The user has pressed the *Mark red SPM chosen value* button and the previously selected coordinate (50, -34, 10) in MNI space, transformed in the plugin to (45, -35, 11) in Talairach space, is marked in the plugin's coordinates list – see Figure 4b.
3. The user has pressed the *Query* button in the *Query Brede database [web browser]* panel (shown on Figure 1) and the webpage with the

query results (related articles) has appeared. The user is now able to compare the obtained results and conclusions with those from the retrieved articles. The webpage results from our example are displayed on Figure 5. The first match from the Brede Database is to a coordinate in *superior temporal gyrus* from an experiment titled *Tics during Tourette's syndrome*. There is a link to the taxonomy of the regions in brain associated with superior temporal gyrus (see Figure 3). Moreover, the user can see the abstract to the article connected with the above mentioned experiment.

4. The user wants to reference some of the articles from the retrieved results in a manuscript. He has selected the bibliographic format, which he is going to use (in this example case 'BibTeX'), pressed *Query* button in the *Query Brede database [export to file(s)]* panel (shown on Figure 1) and the BibTeX file with the references was obtained.
5. The user has discovered a missing feature in the BredeQuery plugin. He thus has pressed the *Feedback* button (Figure 1) and sent a comment to the develop team.

6 FUTURE WORK

The presented plugin for SPM5 is still under development and more features are planned.

It was recently emphasized that there are many separated research communities in neuroscience,

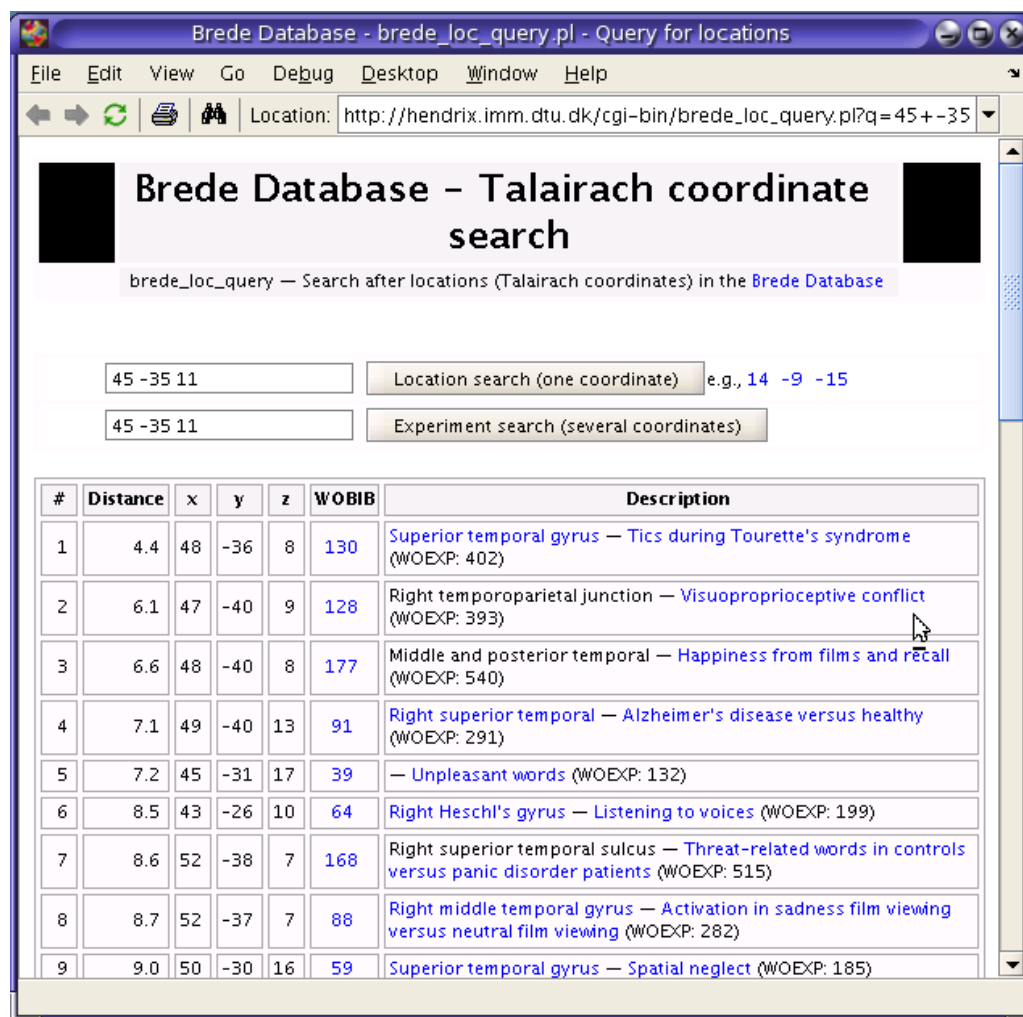


Figure 5: Brede Database query – result displayed in a web browser. List of nearby coordinates to a queried coordinate, displaying distance, the three-dimensional coordinates, the paper identifier, the anatomical label for the retrieved coordinates and short description of the experiment.

which do not want to share or exchange the experimental data (Ascoli, 2006). Researchers have expressed concerns that sharing of data can lead to unfair use (Teeters et al., 2008). However, data sharing is an important current issue in neuroscience (Kennedy, 2007; Liu and Ascoli, 2007) and it is believed that broad data sharing could lead to breakthroughs in our understanding of brain function (Van Horn and Ball, 2008). Invoking online social networks and computer-based communication can support closer relationships and trust (Lampe et al., 2006) hence, reduce the resistance to data sharing.

Consequently, an interesting extension of the functionality of the plugin can be a direct connection from the SPM environment to a neuroscientific

research community, web service or social network. The user would be able to upload the coordinates, results of the analysis, to his own account and save in the assigned server disk space in order to process them later. He can decide whether he wants to keep it private, share only with his research group or alternatively release it as a public resource to all users of the service.

It is also possible to employ the BredeQuery plugin to expand the Brede Database. The increment in number of the articles stored in the database could cause bigger interest from the neuroscientists. They could then be encouraged to register their published or unpublished publications in the database via the BredeQuery plugin together with the reported coordinates and keywords.

7 CONCLUSIONS

In this paper we presented the BredeQuery plugin for SPM5 - an application which offers a direct link from SPM5 to the Brede Database. We provide a mechanism which allows the SPM user to find references to articles which relate to the similar brain activation areas through so-called coordinate-based searching. Moreover, the BredeQuery plugin facilitates the creation of the bibliography files in popular formats.

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